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10/538,434	07/31/2006	Margaret M. Jahn	19603/4252	2309

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EXAMINER	
ZHENG, LI	
ART UNIT	PAPER NUMBER
1638	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,434	JAHN ET AL.	
	Examiner	Art Unit	
	LI ZHENG	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *1-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/17/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-58 are pending.

Election/Restrictions

2. Applicant's election with traverse of Group VI, claims 50-58, including SEQ ID NO: 2 in the reply filed on 1/28/2009 is acknowledged.

Applicants argue that the restriction among Groups III-VI are not proper because Duprat fails to teach or suggest a method of imparting virus resistance to plants by providing nucleic acid molecule encoding a heterologous translation initiation factor eIF4E (response, the paragraph bridging pages 1-2)

The Office contends that different nucleotide sequences and amino acid sequences shown in Groups III-VI are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute different inventive concepts.

As a result, claims 1-49 are withdrawn for being drawn to non-elected inventions.

Claims 50-58 including SEQ ID NO: 2 are examined on the merits.

The requirement is deemed proper and is therefore made FINAL.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See, for example, pages 57 and 58.

Claim Objections

4. Claim 53 is objected to because it contains non-elected inventions.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 58 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn towards a plant seed produced from the plant according to claim 54. Given that one of the parent lines is not defined, it reads on any plant non-transgenic seed found naturally and does not constitute patentable subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brodgex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that claim 58 be amended by reciting that the plant seed comprises a transgene.

Claim Rejections - 35 USC § 112

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 53 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of imparting virus resistance to plant by expressing a heterologous eIF4E in a plant wherein the heterologous eIF4E comprises an amino acid sequence that is at least 85% similar to SEQ ID NO: 2 and containing at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R.

The specification teaches SEQ ID NO: 2 encoded by SEQ ID NO: 1 which is the amino acid sequence of the eIF4E-687 translation initiation factor from Capsicum annuum 'Yolo Wonder' (specification, paragraph [0061]). Alignment of SEQ ID NO: 2 with consensus C. annuum susceptible sequence of RNaky and ECW indicates four mutations including three nonconservative changes, i.e. T51R, P66T and G107R. Other resistant alleles indicate conserved mutations V67E and L79R as well as a specific mutation of D109R.

Applicants do not describe any other proteins having at least 85% similar to SEQ ID NO: 2 and containing at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R that upon heterologous expression, confer resistance to viral infection, except for SEQ ID NO: 2 itself. Applicants also do not correlate the conserved structure to the function of being able to confer resistance to the transgenic plant.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise

definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotides encoding proteins having at least 85% similar to SEQ ID NO: 2 and containing at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R that upon heterologous expression, confer resistance to viral infection. The only species in claimed genus described in the specification are resistant alleles from C. annuum. Applicants also do not disclose structural features common to members of the claimed genus. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Since said genus has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

7. Claims 50-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of imparting virus resistance to plant by expressing a heterologous eIF4E in a plant wherein the heterologous eIF4E comprises an amino acid sequence that is SEQ ID NO: 2 and contains at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R, does not reasonably provide enablement for expressing any heterologous eIF4E in a plant or any heterologous eIF4E comprises an amino acid sequence that is at least 85% similar to SEQ ID NO: 2 and containing at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The instant claims are drawn to a method of imparting virus resistance to plant by expressing a heterologous eIF4E in a plant or wherein the heterologous eIF4E comprises an amino acid sequence that is 85% identical to SEQ ID NO: 2 and contains at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R. The instant claims are also drawn to the plants produced by the method.

The Office interpret the claims to encompass expressing any heterologous eIF4E or any protein that is 85% identical to SEQ ID NO: 2 and contains at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R.

The specification teaches SEQ ID NO: 2 encoded by SEQ ID NO: 1 which is the amino acid sequence of the eIF4E-687 translation initiation factor from Capsicum annuum 'Yolo Wonder' (specification, paragraph [0061]). Alignment of SEQ ID NO: 2 with consensus C. annuum susceptible sequence of RNaky and ECW indicates four mutations including three nonconservative changes, i.e. T51R, P66T and G107R. Other resistant alleles indicate conserved mutations V67E and L79R as well as a specific mutation of D109R.

However, neither the specification nor the prior art teach that expression any heterologous eIF4E would result in increased resistance to virus. On the contrary, the specification teaches that transient expression of a susceptible eIF4E-678 allele in resistance pvr1 plant leaves via Agrobacterium infiltration functionally complemented the resistance phenotype (specification, paragraph [0119]). Further specification

teaches that NIaVPG interaction with eIF4E-687 is not correlated with TEV resistance phenotype (specification, paragraph [0165]). Still further, the specification teaches heterologous expression of eIF4E-RNS and eIF4e-LeS in tomato plant does not confer resistance to TEV (specification, paragraph [0183]). Therefore, Applicants' own data not only provides evidence about the unpredictability of the art, but also confirms that heterologous expression of any eIF4e is not enabled. Therefore, undue experimentation would be required to isolated unexemplified eIF4E genes, to generate overexpression construction, to transform in a heterologous plant, and to test whether overexpression of the unexemplified eIF4E genes would confer viral resistance to the transgenic plant.

Further the specification does not enable any protein that is 85% identical to SEQ ID NO: 2 and contains at least one substitution of at least one amino acid residue of SEQ ID NO: 2 selected from the group consisting of T51A, P66T, V67E, K71R, L79R, G107P and D109R.

Falcon-Perez JM et al. (1999, *J Biol Chem.* 274:23584-90) teach that when twenty-two single amino acid substitutions or deletions were introduced into the nucleotide binding domains, the proposed regulatory domain, and the fourth cytoplasmic loop of the yeast cadmium factor (Ycf1p) vacuolar protein by site-directed mutagenesis, two conserved amino acid residues, Glu (709) and Asp (821), were found to be unnecessary for Ycf1p biogenesis and function.

The state of art also teaches that making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al. (1988, Mol. Cell. Biol. 8:1247-1252) teach that

the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins would have at least 95% identity to the original protein.

Guo et al. (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2).

Therefore, the instant specification fails to provide guidance for which amino acids of SEQ ID NO: 2 can be altered, the type of alteration, and which amino acids must not be changed, to maintain activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a protein that, when overexpressed heterologously, would confer viral resistance to the transgenic plant.

Therefore, given the claim breadth, lack of further guidance and additional working example, unpredictability of the art, undue experimentation would be required for a person skilled in the art to practice the invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Li Zheng/
Examiner, Art Unit 1638